REMARKS

Status of the Claims

Claims 1-12 and 14-80 are pending in the present application. Claims 1-5, 20-37, 39-40, 42-43, and 46-56 were previously withdrawn from consideration as drawn to a non-elected invention. By virtue of this response, claims 60 and 61 have been canceled, claims 6, 9, 10, 14, 15, 19, 44, 57-59, 65, 69, 70, 72, 73, and 79 have been amended, and new claims 81-88 have been added. Accordingly, claims 6-12, 14-19, 38, 41, 44, 45, and 57-59 and 62-88 are currently under examination.

The claim amendments and new claims are supported by the specification as follows: Support for the amendments to claims 6, 14, 15, 72, and 73 may be found, for example, at page 6, lines 13-16. Support for the amendments to claims 9, and 10 may be found, for example, at page 30, lines 16-21. Support for the amendments to claims 14 and 15, and new claims 82-88, may be found, for example, at page 30, line 33 - page 31, line 16, and at page 32, lines 9-19. Support for the amendment to claim 19 may be found, for example, at page 36, lines 16-17. Support for the amendment to claim 44 may be found, for example, at page 14, lines 7-10. Support for the amendment to claims 57, 58, and 70 may be found, for example, at page 57, line 5 - page 58, line 13. Support for the amendment to claim 59 may be found, for example, at page 38, lines 14-20. Support for the amendment to claim 65 may be found, for example, at page 43, lines 21-24. Support for the amendment to claim 69 may be found, for example, at page 36, lines 25-26. The amendment to claim 79 was made, and new claim 81 was added, merely to remove dependence on canceled and multiple dependent claims. The amendments to the specification were made merely to clarify the text of the specification in view of the fact that new figures have been submitted to correct previous typographical errors. No new matter has been added by the foregoing amendments.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached pages are captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**."

With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional applications.

Telephone Interview

Applicants wish to thank Examiners Rawlings and Wortman for extending the courtesy of a telephone interview on July 25, 2002, and for the helpful discussion that ensued. Applicants have given careful consideration to the issues raised in the outstanding Office Action and in the telephone interview, and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Oath/Declaration

Applicants appreciate the statement in the Office Action that it is clear in the declaration as filed that the application to which Applicants claim the benefit of an earlier filing date is U.S. Serial No. 60/035,345, despite the clerical inaccuracy recorded on the declaration. However, in the interest of accuracy, Applicants submit herewith newly executed declarations by the inventors, amended to reflect the correct filing date of January 29, 1996 for application no. 60/035,345. Applicants appreciate the Examiner drawing this point to Applicants' attention.

Objections for Lack of Compliance with the Sequence Rules

The Office Action states that the communication filed June 12, 1998 was not fully responsive to the Office Communication mailed May 8, 1998. The Office Communication of May 8, 1998 was a Notice to Comply with sequence disclosure requirements. Applicants responded on June 12, 1998 by filing a sequence listing, as required by the Notice to Comply. Therefore, Applicants disagree that their response was not fully responsive to the Office

Communication. However, in compliance with the new Notice to Comply that is attached to this Office Action, Applicants submit concurrently with this response a new copy of the sequence listing that was filed on June 12, 1998.

The Notice to Comply states that the amino acid sequence of Figure 1 does not match the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:2 of the Sequence Listing. As an initial matter, Applicants note that the amino acid sequence of Figure 1 cannot "match" the sequence of SEQ ID NO:1, because SEQ ID NO:1 is a polynucleotide sequence. The cDNA sequence depicted in Figure 1 is correct and corresponds identically to SEQ ID NO:1 (see page 5, lines 20-21). The amino acid sequence depicted in Figure 1 contains two typographical errors, which are set forth with the errors as they appear in Figure 1 in SEQ ID NO:58, and in corrected form in SEQ ID NO:2 (see page 5, lines 22-23 and page 69, lines 15-21 of the specification). Therefore, although the sequence set forth in Figure 1 does not match SEQ ID NO:2, it nevertheless matches SEQ ID NO:58. The specification also discloses that there is a typographical error in the sequence depicted in Figure 3A (see page 5, lines 28-29, and page 69, lines 18-19).

In the telephone interview of July 25, 2002, Examiners Rawlings and Wortman suggested amending the figures to correct the clerical errors in the figures that were filed with the application. Accordingly, attached herewith are corrected drawings for Figure 1 and 3A, with corrections made so that the amino acid sequences correspond to the sequences in SEQ ID NO:2. In accordance with MPEP § 608.02(p), the changes to the figures are indicated in red ink on attached copies of the figures as originally submitted. The corrected sequences are identical to the sequences that were originally submitted as SEQ ID NO:2. The corrections are made merely to correct errors that would be obvious to one of skill in the art, *i.e.* the nucleotide triplet GCC encodes the amino acid Alanine (A), not Threonine (T), and the nucleotide triple GAA encodes Glutamic acid (E), not Glycine (G). The MPEP states, "Amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of error in the specification, but also the appropriate correction." MPEP § 2163.07,

citing *In re Oda*, 443 F.2d 1200 (CCPA 1971). Accordingly, no new matter has been added by the changes to the figures.

Withdrawn Claim Rejections

Applicants acknowledge with appreciation the withdrawal of previous rejections, as noted on pages 5-12 of the Office Action, such as the rejections under 35 U.S.C. §§ 101, 102(b), (e), and (f), and 112, first and second paragraphs, and the rejection of claim 19 over claim 3 of co-pending application no. 08/766,350.

Rejections under 35 U.S.C. §101

Claims 6-12, 59, 62, 63, and 72-75

Claims 6-12, 59, 62, 63, and 72-75 are rejected under 35 U.S.C. §101 as allegedly directed to non-statutory subject matter.

Applicants respectfully disagree with the statement in the Office Action that the subject matter of these claims encompasses naturally-occurring products because the hybridoma that produces monoclonal antibody 11D10 naturally produces polypeptides that fulfill the limitations of the claims and because the hybridoma was derived from a naturally-occurring lymphocyte. Office Action, page 22. Applicants respectfully submit and reiterate that a hybridoma is not a naturally-occurring product, because by definition it is produced *in vitro* by fusion of a lymphocyte with an immortalized cell. The *in vitro* fusion is a manipulation that removes the lymphocyte from its natural environment and alters it so that it can grow in culture, which it cannot do in the absence of the fusion. Once altered by the fusion, the lymphocyte is no longer naturally-occurring.

The Office Action states that amending the claims to recite the term "isolated," "purified," or "recombinant" will obviate the rejection. Although Applicants disagree that the claims encompass naturally-occurring products, Applicants have amended the claims to recite the term "isolated," solely to expedite prosecution.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 101.

Claims 14 and 15

Claims 14 and 15 are rejected under 35 U.S.C. § 101 as allegedly not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse this rejection.

As discussed during the telephone interview, the specification discloses several specific and substantial utilities that are credible. Any one of these uses satisfies the utility requirement. For example, the specification discloses use of polynucleotides of the invention in expression systems for the recombinant production of 11D10 or 11D10 fragments, as hybridization probes to assay for the presence of 11D10 polynucleotide (or related) sequences in a sample, as amplification primers, and as vaccines or for gene therapy. Page 36, lines 31-36. Each of these uses is described in detail on pages 36-37 of the specification. The polynucleotides relate to a specific, useful antibody, namely 11D10.

A specific, substantial, and credible utility disclosed in the specification is use of polynucleotides of the invention as primers for amplification of polynucleotides encoding 11D10 or a fragment thereof in an amplification system such as PCR. Page 36, line 37 - page 37, line 3. This use is specific (primers are specific for the sequences to be amplified), substantial (amplification of polynucleotides is a "real world" use that is well established in the art), and credible (believable, because such amplification procedures are well established).

The specification also discloses use of polynucleotides of the invention as hybridization probes for detection of, for example, the presence of 11D10 polynucleotides in a cell. This use is specific (probes are specific for the sequences to which they hybridize), substantial (use of probes for detection of polynucleotide sequences is a "real world" use that is well established in the art), and credible (believable, because such hybridization procedures are well established). Applicants disagree with the statement in the Office Action that use of a polynucleotide as a

probe "lacks specificity and is not considered substantial . . .[s]ince such a utility generally applies to any nucleic acid molecule." The Office Action further states that this asserted utility is "generic and trivial." Office Action, page 22. Applicants disagree that probes lack specificity. Probes by definition are specific for the sequences to which they are capable of hybridizing. Thus, this utility is not "generic and trivial," because it is directed to specific, rather than "generic," polynucleotide sequences. Further, use of a polynucleotide as a probe is a substantial use. The Examiner's assertion that this use is "generic and trivial" is not the correct standard for determining whether a use is substantial. The correct test is whether the asserted utility defines a "real world" use (*i.e.*, whether the utility would require further research to identify or confirm a "real world" context of use). MPEP § 2107.01. The Office Action asserts that "[i]t is common and routine to use a portion of a nucleic acid molecule as a probe to detect or quantify a nucleic acid comprising the polynucleotide sequence of the probe." Office Action, page 22. Therefore, the fact that such uses for polynucleotides are "common and routine" suggests that this use is a "real world," well-accepted utility, and is therefore substantial. Certainly, probing for a specific, useful sequence is a "real world" use.

A further utility disclosed in the specification is use of polynucleotides of the invention in expression systems for the recombinant production of 11D10 antibody or fragments, or recombinant forms of 11D10 and 11D10 polypeptides, such as hybrids, chimeras, single chain variants and fusion proteins containing other components such as cytokines. Page 37, lines 15-19. Such a use is specific, because expression is directed to particular, defined sequences. The use is also substantial, because the polynucleotides encode useful polypeptides, namely 11D10 polypeptides (including 11D10 antibody and fragments thereof) or useful recombinant forms of 11D10. This utility is also credible, because recombinant methods and use of such expression systems is well-established and routine in the art.

The specification also discloses use of 11D10 polynucleotides as DNA vaccines. Page 37, lines 22-35. Such vaccines may be used to generate a specific immune response to the 11D10 antigen, encoded by the polynucleotide of the vaccine. This utility is specific (*i.e.*, generation of

an immune response to the particular 11D10 antigen encoded by the 11D10 polynucleotide of the vaccine), substantial (*i.e.*, useful in methods of treatment for disease conditions), and credible (*i.e.*, well-known in the art).

In order to satisfy the statutory requirement for utility, Applicants need to provide only one credible assertion of specific and substantial utility. MPEP § 2107. As discussed above, Applicants have disclosed several specific, substantial, and credible utilities that are well-established uses for polynucleotides. Therefore, the presently-claimed invention satisfies the utility requirement for patentability.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 101.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 14 and 15

Claims 14 and 15 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled because they are allegedly not supported by a specific, substantial, and credible, or well-established utility. Applicants respectfully traverse this rejection.

As discussed above, the invention is supported by a number of specific, substantial, and credible utilities, such as use as probes or amplification primers. As such, the "use" requirement of §112, first paragraph, is satisfied and this rejection may be properly withdrawn. Further, descriptions of how to make and use polynucleotides of the invention for such purposes may be found in the specification, for example, on page 33, line 23 - page 34, line 6, and on page 36, line 31 - page 38, line 10. Thus, it would not require undue experimentation for one of skill in the art to practice the disclosed utilities of the invention.

The Office Action states that the invention of claims 14 and 15 is not enabled because the specification fails to provide working examples of use of the invention to elicit an anti-HMFG immunological response in a mammal or to induce antitumor immunity in a mammal. Office Action, page 24. Applicants note that claims 14 and 15 do not recite these limitations. Claims

14 and 15, as amended, are directed to an isolated polynucleotide comprising a region of at least 100 contiguous nucleotides of the sequence contained in SEQ ID NO:1 or at least 75 contiguous nucleotides of the sequence contained in SEQ ID NO:3, respectively. Therefore, an enablement rejection based on an alleged lack of exemplification of an anti-HMFG immune response or antitumor immunity is inapplicable to the claimed invention.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph. Applicants note that withdrawal of the rejection of claims 14 and 15 under 35 U.S.C. §101, discussed above, would render this rejection moot.

Claims 6-12, 16-19, 38, 41, 44, 45, 59-64, 66, 70, 71, and 76-80

Claims 6-12, 16-19, 38, 41, 44, 45, 59-64, 66, 70, 71, and 76-80 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement for a polynucleotide that encodes a polypeptide that is capable of eliciting an anti-HMFG immunological response in a mammal. Applicants respectfully traverse this rejection.

Applicants maintain that the specification provides adequate guidance to enable one of skill in the art to make and use the claimed invention without undue experimentation. For example, the specification provides methods for making 11D10 polynucleotides encoding fragments of 11D10 and testing these polypeptides encoded by such fragments for the immunological function of interest. The specification provides examples of methods for making polynucleotides of the invention, for example by chemical synthesis, recombinant methods, or PCR amplification (see page 33, line 23 - page 34, line 6). Such methods are well known in the art. It would be a matter of routine for a skilled artisan to make a polynucleotide that encodes a polypeptide that comprises an immunoglobulin variable region containing the three heavy chain or light chain CDRs, using conventional recombinant or synthetic techniques.

The specification also provides methods for testing the polypeptides of the invention for an ability to elicit an anti-HMFG immunological response in a mammal. An "immunological

response" includes a humoral and/or cellular response. Page 14, lines 25-26. Functional assays for characterization of an immunological response are provided in the specification, for example on page 48, line 33 - page 51, line 12. Such assays are routine within the art. Further, a method for testing recombinant 11D10 polynucleotides for their ability to stimulate an immune response in a mammal is provided in Example 9 of the specification. Page 90, line 31 - page 91, line 8.

The Office Action states that the skilled artisan would not have a reasonable expectation of successfully producing and using the claimed invention, which includes a multitude of potentially non-working embodiments. Office Action, page 26. The Examiner has apparently confused the standard for obviousness with the standard for enablement in requiring a "reasonable expectation of success." This is the standard for obviousness, not enablement. Further, even if, for the sake of argument, the claims encompass non-working embodiments, this does not render a claim nonenabled. MPEP § 2164.08(b). The court in *Atlas Powder Co. v. Du Pont*, 750 F.2d 1569, 1576 (Fed. Cir. 1984) stated that "[i]t is not a function of the claims to specifically exclude . . . possible inoperative substances." The MPEP states that "[t]he standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with the expenditure of no more effort than is normally required in the art." MPEP 2164.08(b). As discussed above, methods for determining which embodiments are operative (*i.e.*, assays for elicitation of a humoral or cellular immune response) are a matter of routine in the art. Thus, a skilled artisan would readily be able to make and use the invention based upon the disclosure in the specification.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Claims 6-19, 38, 41, 44, 45, 57-63, 66, 70, and 72-80

Claims 6-19, 38, 41, 44, 45, 57-63, 66, 70, and 72-80 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not supported by adequate written description for a polynucleotide

comprising a sequence encoding a polypeptide that comprises an immunoglobulin variable region containing the three light chain or heavy chain CDRs of antibody 11D10.

The Office Action states that the claims encompass a genus of nucleic acid molecules, but the written description allegedly only sets forth the structures of two species of the claimed genus, SEQ ID NOs: 1 and 3, and therefore, the written description is not reasonably commensurate with the claims. Office Action, page 35. Applicants note that claim embodiments reciting a polynucleotide encoding an amino acid sequence are supported by the amino acid sequences that are disclosed in the specification. There is no requirement in the law to expressly call out each polynucleotide sequence. As for claim embodiments which are fragments of a polynucleotide sequence, these are implicitly described within the polynucleotide sequence itself.

Applicants respectfully point out that it is a well-established principle of patent law that "patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art." *In re Vaeck*, 947 F.2d 488, 496 (Fed. Cir. 1991). In *In re Angstadt*, the Court of Customs and Patent Appeals considered the issue of whether section 112 requires disclosure of a test with every species covered by a claim and concluded that requirement of such a complete disclosure would necessitate a patent application with thousands of examples and "would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments." *In re Angstadt*, 537 F.2d 498, 502 (CCPA 1976). The court concluded that such a requirement would be against public policy because it would have the effect of "depriving inventors of claims which adequately protect them and [would limit] them to claims which practically invite appropriation of the invention while avoiding infringement[, which would] inevitably [have] the effect of suppressing disclosure." *Id.* at 504. In conclusion, based on the foregoing, Applicants traverse the suggestion that the disclosure of species in the specification is insufficient written description for the claimed genus.

The Examiner relies upon the decision in *The Regents of the University of California v. Eli Lilly*, 119 F.3d 1559 (Fed. Cir. 1997). However, this case is inapplicable here, and the Examiner fails to apply the holding in *Eli Lilly* to the disclosure of the instant specification. In

Eli Lilly, the court affirmed that "every species in a genus need not be described in order that a genus meet the written description requirement." *Id.* at 1568. The court stated that "[a]n adequate written description of a DNA . . . 'requires a precise definition, such as by structure, formula, chemical name, or physical properties.' *Id.* at 1566. The court indicated that *structural* characteristics, such as nucleotide sequence information, would provide adequate disclosure to satisfy the written description requirement. *Id.* at 1567. The claims at issue in *Eli Lilly* recited a reverse transcript of an mRNA encoding human insulin, and provided a method for obtaining such a cDNA via a prophetic example in the specification, but did not provide the nucleotide sequence of the cDNA. Thus, the claims at issue in *Eli Lilly* described the cDNA only in terms of function, rather than structure. The written description issue in that case revolved around a complete lack of structural description for a claimed genus of polynucleotides. In contrast, the present claims are supported by structural information, in particular the CDR polynucleotide sequences provided in SEQ ID NO:1 and SEQ ID NO:3 for the light and heavy chain variable regions, respectively, of antibody 11D10. The structural recitation of the three light or heavy chain CDRs also provides recitation of structural features common to the members of the genus.

In the telephone interview of July 25, 2002 and in the Office Action (page 35), the Examiner expressed concern that the claims as written encompassed genomic DNA. The claims as amended recite an "isolated" polynucleotide, which is defined in the specification as a polynucleotide that is "substantially free of the materials with which it is associated in nature." Page 16, lines 13-14. Thus, the claims as amended do not encompass genomic DNA.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Claims 6-12, 16-19, 38, 41, 44, 45, 59-71, and 76-80

Claims 6-12, 16-19, 38, 41, 44, 45, 59-71, and 76-80 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not supported by adequate written description with respect to the phrase "progeny thereof."

The claims as amended no longer recite the phrase "progeny thereof," rendering this rejection moot.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Claims 6-12, 16-19, 38, 41, 44, 45, 59-71, and 76-80

Claim 6-12, 16-19, 38, 41, 44, 45, 59-71, and 76-80 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not supported by adequate written description with respect to the phrase "capable of eliciting an anti-HMFG immunological response." The Examiner states that the disclosure on page 4, lines 5-6 of the specification that "the invention . . . includes polynucleotides comprising a sequence encoding a polypeptide having immunological activity of monoclonal anti-idiotype antibody 11D10" does not provide adequate support for the phrase "capable of eliciting an anti-HMFG immunological response." Office Action, pages 40-41.

Applicants respectfully traverse this rejection and note that the specification provides direct, literal support for the phrase "capable of eliciting an anti-HMFG immunological response" on page 65, lines 3-4. In addition, support is provided via the disclosure of immunological activities encompassed by the invention. For example, on page 4, lines 5-6, the specification discloses that "the invention . . . includes polynucleotides comprising a sequence encoding a polypeptide having immunological activity of monoclonal anti-idiotype antibody 11D10." Applicants note that "immunological activity" is defined on page 11, lines 24-29, as including, *inter alia*, "ability to elicit a specific immune response." Thus, having immunological activity of monoclonal anti-idiotype antibody 11D10 includes the ability to elicit an immunological response that is specific to 11D10, *i.e.*, an anti-HMFG immunological response. Page 3, lines 28-29. Further, the specification discloses identification and characterization of a polypeptide fragment of 11D10 as having, *inter alia*, an "ability to elicit an immune response (i.e., humoral and/or cellular response, *preferably an immune response that is anti-HMFG*)." Page 14, lines 23-27, emphasis added.

In conclusion, the language "capable of eliciting an anti-HMFG immunological response" is literally supported in the specification, as discussed above. The claims already recite the explicit language of the specification. Second, even if the phrase were not literally supported, the language in the specification and claims do not need to be identical. Applicants note that the standard for written description is whether the disclosure would convey to a skilled artisan that the applicant was in possession of the invention as of the filing date. MPEP § 2163.02. Support in the specification may be express, implicit, or inherent. MPEP § 2163(I)(B). The statement in the Office Action that "amending the claims to recite the explicit language of the specification could obviate the basis of this rejection" (Office Action, page 41) is contrary to the legal standard for written description. Even if the phrase at issue were not literally supported, the language in the specification and claims do not need to be identical. However, as discussed above, the claims already recite the explicit language of the specification, rendering the Examiner's statement and rejection moot.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Claims 44, 45, 57, 58, 79, and 80

Claims 44, 45, and 79 are objected to and claims 57, 58, and 80 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not supported by adequate written description for the term "live virus." Applicants respectfully traverse this rejection.

The Office Action indicates that pointing to the disclosure in the specification which supports the claim term "live virus" will obviate this rejection. Office Action, pages 41-42. Page 55, line 13 of the specification discloses use of polynucleotides of the invention in "live or attenuated viruses." Thus, the specification provides express support for the term "live virus."

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Claims 57 and 58

Claims 57 and 58 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not supported by adequate written description. Applicants respectfully traverse this rejection.

Claims 57 and 58, as amended, recite a kit for detection or quantitation of a polynucleotide which comprises a sequence encoding a variable region of antibody 11D10 or a portion thereof, wherein the kit comprises the polynucleotide of claim 14 or 15 in packaging. The Office Action states that the specification does not appear to provide support for a polynucleotide that comprises a sequence encoding a variable region of antibody 11D10 or a portion thereof. Office Action, page 42. Applicants note that the specification recites that kits of the invention "can be used for detection or quantitation of a *polynucleotide that comprises a polynucleotide encoding a variable region of 11D10 or a portion thereof.*" Page 58, lines 3-5, emphasis added.

The Office Action states that "amending the claims to recite the explicit language of the specification could obviate the basis of this rejection." Office Action, page 42. The claims already recite this explicit language, which should render this rejection moot. However, *in haec verba* support is not required for satisfaction of the written description requirement. The specification conveys to a skilled artisan that Applicants were in possession of the subject matter of claims 57 and 58 at the time of filing, which is the legal standard for written description. One of skill in the art would understand that a *sequence* encoding a variable region of antibody 11D10 or a portion thereof, as recited in the claims, which recite that the kit is for detection or quantitation of a polynucleotide, refers to a *polynucleotide* encoding a variable region of 11D10 or a portion thereof, as recited in the specification. Thus claims 57 and 58 are adequately supported by the disclosure in the specification.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 6-12, 16-19, 38, 41, 44, 45, 59-71, and 57-80

Claims 6-12, 16-19, 38, 41, 44, 45, 59-71, and 57-80 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite due to recitation of the term "capable of." Applicants respectfully traverse this rejection.

Applicants submit that one of skill in the art would understand the term "capable" to mean "having the ability, capacity, or power to do something," according to its dictionary definition. Webster's New Ideal Dictionary, ©1973. Applicants disagree with the statement in the Office Action that the claim is vague and indefinite because it cannot be ascertained whether the claim requires the polypeptide encoded by the claimed polynucleotide to be actually eliciting an immunological response or to merely have the potential of doing so. Office Action, pages 42-43. The polypeptide cannot elicit an immune response until administered to a mammal. Until such administration, the polypeptide is only capable of eliciting the response. It would be understood by one of skill in the art that the capacity of the polypeptide to elicit an immunological response cannot be fully realized until placed within proximity of an immune system of an individual to which it is administered. Therefore, the term "capable of" is not indefinite and would apprise one of skill in the art of the metes and bounds of the claimed invention. Applicants note that the phrase "capable of eliciting an immunological response in a mammal" may be found in other claims that have been allowed and issued by the Office, for example, in U.S. Patents 5,935,821 and 5,977,316.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claims 9, 10, and 78

Claims 9, 10, and 78 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite due to recitation of the phrase "wherein the immunoglobulin variable region is

contained in [SEQ ID NO:2 or SEQ ID NO:4]," because it is allegedly not clear whether the claims refer to the light chain or heavy chain variable region.

Applicants respectfully maintain that the claims as written define which variable region is encompassed, since the claims recite that the variable region is contained in SEQ ID NO:2 or SEQ ID NO:4, which are the amino acid sequences of the light and heavy chain variable regions, respectfully. However, in the interest of expediting prosecution, Applicants have amended claims 9 and 10 to recite that the immunoglobulin variable region is the "light chain" or "heavy chain" variable region, which the Office Action states will obviate the rejection.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claims 11, 12, and 78

Claims 11, 12, and 78 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite due to recitation of the phrase "wherein the encoding sequence is contained in the variable region encoding sequence in [SEQ ID NO:1 or SEQ ID NO:3]." Applicants respectfully traverse this rejection.

Applicants disagree with the statement in the Office Action that an encoding sequence within the scope of the claims "would necessarily comprise the *entire* variable region encoding sequence to encode an immunoglobulin variable region of an antibody." Office Action, page 44. Claim 6, from which claims 11 and 12 depend, recites an isolated polynucleotide encoding a polypeptide capable of eliciting an anti-HMFG immunological response in a mammal, wherein the polypeptide comprises an immunoglobulin variable region containing the three light chain or heavy chain CDRs. A polynucleotide, to be within the scope of claim 6, must encode a polypeptide capable of eliciting an anti-HMFG response and must contain three light chain or heavy chain CDRs. There is no recitation in claim 6 of a polypeptide which comprises an entire variable region of 11D10. As long as the polypeptide (1) can elicit an anti-HMFG immune response, and (2) includes three CDRs, it falls within the scope of the claim. Polynucleotides

encoding such polypeptides may thus be *contained in* SEQ ID NO:1 or SEQ ID NO:3, rather than comprising the entire light or heavy chain variable region set forth in SEQ ID NO:1 or SEQ ID NO:3. Since polypeptides encoded by the encoding sequence must meet the two requirements set forth in claim 6, it would be clear to one of skill in the art which encoding sequences are encompassed by claims 11 and 12.

Applicants note that language identical to the language in claims 11 and 12 has been allowed and issued by the Office in other claims, for example in U.S. Patent No. 5,935,821.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claims 41, 44, 45, 61, 66, and 79

Claims 41, 44, 45, 61, 66, and 79 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite due to recitation of the phrase "[an] immunogenic composition comprising the polynucleotide of claim 6." The Office Action states that it appears that the invention provides a polypeptide that is immunogenic rather than a polynucleotide that is immunogenic. Office Action, page 44. Applicants respectfully traverse this rejection.

Applicants submit that a composition that comprises the polynucleotide of claim 6, as claimed in claim 41, may be an immunogenic composition by virtue of the fact that it encodes and expresses a polypeptide that is useful for eliciting an anti-HMFG immunological response. The specification defines an "immunogenic" compound as "able to elicit a specific immune response." Page 11, lines 33-34. One of skill in the art would readily appreciate and understand that a composition that gives rise to an immune response is immunogenic. Thus, a composition comprising the polynucleotide of claim 6 is immunogenic if a polypeptide expressed therefrom elicits an anti-HMFG immunological response. The metes and bounds of this claim are clear as written.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claims 44 and 45

Claims 44 and 45 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite due to recitation of the terms "live virus" and "viral expression vector." Applicants respectfully traverse this rejection.

The specification discloses use of 11D10 polynucleotides in "live or attenuated viruses" or "viral vectors which can express an encoded 11D10 polypeptide" (*i.e.*, a viral expression vector) (page 55, lines 13-14), thereby providing direct support for the terms used in claim 44. The Office Action states that the only disclosed example of a vector that could be used to elicit an immune response in a mammal is vaccinia. Office Action, page 45. Applicants respectfully disagree and submit that this in not an appropriate ground for an indefiniteness rejection. However, Applicants note that the specification discloses examples of such vectors other than vaccinia, for example adenovirus, adeno-associated retroviruses (AAV), and SV40, in addition to vaccinia. Page 55, line 15. Applicants further note that the term "viral expression vector" has previously been deemed by the Office to be acceptable and may be found in issued claims, for example, claims 13 and 19 of U.S. Patent No. 5,935,821. "Live virus" and "viral expression vector" are terms that are well understood by those of skill in the art, particularly in view of the examples set forth on page 55. Applicants submit that the metes and bounds of claims 44 and 45 are clear as written. However, Applicants have amended claim 44 to recite "live recombinant virus," solely to clarify the claim.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claims 59, 77, and 78

Claims 59, 77, and 78 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite due to recitation of the phrase "wherein antibody 11D10 has the light and heavy chain

variable region sequences contained in SEQ ID NO:2 and SEQ ID NO:4, respectively." Applicants respectfully traverse this rejection.

The Office Action states that the claims are indefinite because it is unclear to which light and heavy chain variable region sequences contained in SEQ ID NO:2 and SEQ ID NO:4 the claim refers. Office Action, page 45. Applicants note that SEQ ID NO:2 and SEQ ID NO:4 depict the amino acid sequences of the light and heavy chain variable regions, respectively, of antibody 11D10. The claim is clear because it recites that antibody 11D10 has (*i.e.*, encompasses) the light and heavy chain variable region sequences contained in these two SEQ IDs. The Examiner suggests amending the claim to recite "wherein antibody 11D10 has the light and heavy chain variable region encoding sequences of SEQ ID NO:2 and SEQ ID NO:4, respectively." Office Action, page 45. Applicants note that SEQ ID NOs: 2 and 4 do not represent encoding sequences, but rather represent the amino acid sequences encoded by the encoding sequences represented by SEQ ID NOs:1 and 3, which depict the polynucleotide sequences for the light and heavy chain variable regions, respectively, of antibody 11D10. Therefore, "encoding sequences" would be improper terminology to add to a claim referring to the amino acid sequences contained in SEQ ID NOs: 2 and 4. In view of the foregoing, Applicants submit that claim 59 is clear as written such that one of skill in the art would be apprised of the metes and bounds of the claimed invention.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claims 57, 58, and 80

Claims 57, 58, and 80 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite due to recitation of the phrase "a kit for detection or quantitation of a polynucleotide comprising a polynucleotide which comprises a sequence encoding a variable region of antibody 11D10 or a portion thereof, said kit comprising the *polynucleotide* (emphasis added)," because it

is allegedly unclear which of the two previously-recited polynucleotides the emphasized polynucleotide refers to.

Applicants respectfully point out that the term "polynucleotide" at issue in claims 57 and 58 refers to the polynucleotide of claim 14 or 15, respectively, rather than the two previous recitations of the term "polynucleotide," as asserted in the Office Action. However, in the interest of clarifying the claims, Applicants have amended claims 57 and 58 to delete the first recitation of the term "polynucleotide."

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claims 57, 58, 70, and 80

Claims 57, 58, 70, and 80 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite due to recitation of the phrase "suitable packaging."

Applicants respectfully maintain that "suitable" is an appropriate claim term (see, *e.g.*, issued U.S. Patent No. 5,977,316), and that types of materials that would provide suitable packaging for a kit would be readily apparent to one of skill in the art. However, in the interest of expediting prosecution, Applicants have deleted the term "suitable" from the claims, which the Office Action states will obviate the rejection.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claims 60, 61, and 79

Claims 60, 61, and 79 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite due to recitation of the phrase "further comprising an amount of polynucleotide sufficient to elicit an anti-HMFG immunological response." Claims 60 and 61 have been canceled, rendering the rejection moot.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claims 64, 65, 71, and 76-79

Claims 64, 65, 71, and 76-79 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite due to recitation of the phrase "an immunoglobulin variable region containing the three light chain CDRs of antibody 11D10 and an immunoglobulin variable region containing the three heavy chain CDRs of antibody 11D10." The Office Action states that the claim is unclear because the order of the CDRs is not specified. Office Action, pages 46-47. Applicants respectfully traverse this rejection.

Applicants maintain that the claims are clear as written and note that claim language identical to the language at issue has been previously allowed by the Office and appears in issued claims, for example in U.S. Patent No. 5,935,821. The order of the CDRs does not need to be the same as the order in the variable regions of antibody 11D10, and does not need to be specified in the claims. Claim 64 is dependent upon claim 6, which requires polynucleotides of the invention to encode a polypeptide that is capable of eliciting an anti-HMFG immunological response. Polynucleotides encoding the CDRs of 11D10, the sequences for which are provided in the specification (*e.g.*, Figures 3A and 3B), could be readily recombined by one of skill in the art, as a matter of routine, to form a recombinant or chimeric polynucleotide encoding a polypeptide as specified by claim 6. To fall within the scope of the claims, such polynucleotides must encode a polypeptide that is capable of eliciting an anti-HMFG immunological response. Therefore, one of skill in the art would be apprised of the metes and bounds of the claimed invention, because any polynucleotide within the scope of the claims would encode a polypeptide that is capable of eliciting a specific immune response and would include all six CDRs of antibody 11D10. Also, to the extent a T cell response is elicited, such responses are well known in the art to be elicited by and directed to small fragments, so the CDRs would not

necessarily need to be in the same order as in the native antibody to elicit a T cell immune response.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claims 65, 76, 78, and 79

Claims 65, 76, 78, and 79 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite due to recitation of the term "linked polypeptide."

To correct a typographical error, Applicants have amended claim 65 to recite "linker" instead of "linked," which the Office Action states will obviate the rejection. Applicants appreciate the Examiner pointing out this clerical error.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claims 72-75

Claims 72-75 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite due to recitation of the phrase "an immunoglobulin variable region containing the three light [or heavy] chain CDRs in [SEQ ID NO:2 or SEQ ID NO:4]." Applicants respectfully traverse this rejection. The Office Action states that the claim is unclear because the order of the CDRs is not specified. Office Action, page 47. Applicants respectfully traverse this rejection.

Applicants maintain that the claims are clear as written and note that claim language identical to the language at issue has been previously allowed by the Office and appears in issued claims, for example in U.S. Patent No. 5,935,821. As discussed above, the order of the CDRs does not need to be in the same order as the variable regions of 11D10, and does not need to be specified in the claims. The CDRs of antibody 11D10 are set forth in the specification, for example in Figures 3A and 3B. Therefore, one of skill in the art would be apprised of the metes and bounds of the claimed invention, because polynucleotides that fall within the scope of the

claims could be readily determined by a comparison of the amino acid sequence encoded by a particular polynucleotide with the amino acid sequences of the CDRs set forth in Figure 3A or 3B. A polynucleotide that encodes an immunoglobulin variable region that includes the three light chain or heavy chain variable region CDRs, as recited in claims 72 and 73, would be readily ascertainable by one of skill in the art.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claims 76-80

Claims 76-80 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite due to recitation of the phrase "any of claims." Applicants respectfully traverse this rejection.

MPEP § 608.01(n) lists examples of acceptable wording for multiple dependent claims. Included in this list is a claim that recites "any of claims." Further, upon a search of the U.S. Patent and Trademark Office online database, Applicants' representative found 3,589 U.S. patents with the phrase "any of claims" in the claims of patents issued between 1996 and 2002. Therefore, the language of claims 76-80 is within the guidelines set forth by the Patent Office and is appropriate and clear as written.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claims 14, 15, and 72-75

Claims 14, 15, and 72-75 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly failing to set forth the subject matter which Applicants regard as their invention. Applicants respectfully traverse this rejection.

Applicants disagree with the statement in the Office Action that the subject matter of the claims cannot be distinguished from naturally occurring products and therefore claims 14, 15,

and 72-75 fail to correspond in scope with that which Applicants regard as the invention (Office Action, page 48). Applicants reiterate their previous argument that the claimed polynucleotide sequences of the invention are not naturally-occurring in the sense that they arose due to manipulations to make an antibody-producing hybridoma, which does not occur in nature. Applicants also point out that U.S. Pat. No. 5,934,821, claiming polynucleotides which also arose from production of a hybridoma (see U.S. Pat. No. 5,612,030), does not contain the term "isolated", nor did the Office raise this rejection in that case. However, in the interest of expediting prosecution, Applicants have amended the claims to recite an "isolated" polynucleotide, which the Office Action states is sufficient to distinguish the subject matter of the claims from naturally-occurring products.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Rejection under 35 U.S.C. § 102(a)

Claims 6-12, 14, 15, 38, 41, 57-63, 70, and 72-80 are rejected under 35 U.S.C. § 102(a) as allegedly anticipated by Chakraborty et al., 1995, *J. Immunotherapy* 18:95-103. Applicants respectfully traverse this rejection.

Applicants submit herewith a declaration by Malaya Chatterjee outlining the roles and contributions of the non-inventor authors of the cited reference. The work reported in Chakraborty et al. was done in the laboratory of the inventors, under their direction and supervision, and was published less than one year prior to the filing of the instant application. Therefore, Chakraborty et al. is not available as a § 102(a) reference. During the telephone interview, the Examiners indicated that the attached declaration would be acceptable to remove Chakraborty et al. as §102(a) reference.

Applicants disagree with the Examiner's statement that the teachings of Chakraborty et al. anticipate the claimed invention because "[t]he polynucleotides encoding the light and heavy chains of monoclonal antibody 11D10 are inherent features of the hybridoma" (Office Action,

page 48). Even though this reference is not available under §102(a), as discussed above, Applicants reiterate the arguments made previously in the responses to paper nos. 15 and 24. Chakraborty et al. is not enabling with respect to the claimed invention because the polynucleotides encoding 11D10 are not disclosed and further, the hybridoma producing 11D10 antibody was not available to the public. Since it would not be possible to derive the polynucleotide sequences encoding 11D10 antibody as claimed from this reference, the teachings of Chakraborty et al. would not enable one of skill in the art to make and use the claimed invention.

Applicants also note that the claims as amended recite an "isolated" polynucleotide, which the Office Action indicates will obviate the rejection. However, as stated above, Applicants reiterate that this reference, as well as being unavailable as art under § 102(a), is also non-enabling for the claimed polynucleotides, and the record has ample factual evidence in this regard.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(a).

Rejections under 35 U.S.C. § 103(a)

Claims 6-12, 14-19, 38, 41, 44, 45, 57-66, and 70-80 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Bhattacharya-Chatterjee et al., 1994, in *Antigen and Antibody Molecular Engineering in Breast Cancer Diagnosis and Treatment*, Ceriani, R.L., ed., Plenum Press, New York, pp. 139-148, in view of Chakraborty et al., *Proceedings of the American Association for Cancer Research*, 35:497, Abstract No. 2963, and further in view of Kennedy et al., 1985, *Biotechniques* 3:404-410, and WO 94/11508-A2 (May 26, 1994) or Spooner et al., 1995, *Gene Therapy* 2:173-180 and Stevenson et al., 1995, *Immunological Reviews* 145:211-228 and in still further view of Herlyn et al., 1995, *Hybridoma* 14:159-166. Applicants respectfully traverse this rejection.

A prima facie case for obviousness requires, *inter alia*, that prior art references, when combined, must teach or suggest all claim limitations. MPEP § 2143. The cited references do not teach, either singly or in combination, an isolated polynucleotide that encodes a polypeptide comprising the three light chain or heavy chain CDRs of antibody 11D10, as recited in the present claims. Applicants note that Bhattacharya-Chatterjee et al. and Chakraborty et al. were previously cited as §102(b) references against claims 16-19, 44, and 45 (paper nos. 15 and 24). The rejections based on these references have been withdrawn (Office Action, pages 7-8). Thus, neither of these references anticipates the claims. As discussed below, the combination of these two references with the other cited references does not provide the missing information and thus does not render the claimed invention obvious.

Applicants reiterate the points made in responses (accompanied by declarations) to paper nos. 15 and 24 that neither Bhattacharya et al. nor Chakraborty et al. is an enabling reference and that the 11D10 antibody was not provided to the public prior to the filing date, and refer the Examiner to these documents. Specifically, Bhattacharya-Chatterjee et al. and Chakraborty et al., which disclose that a hybridoma named "11D10" produces antibody 11D10 and use of antibody 11D10 to induce an anti-HMFG immune response in monkeys, respectively, do not disclose either the polypeptide sequences of 11D10, or the polynucleotide sequences that encode the polypeptides. As provided in the record, based on the nature of antibody formation, disclosure of how antibody 11D10 was generated does not provide an enabling disclosure of the amino acid sequence of 11D10, or polynucleotides encoding 11D10. These points have been considered and accepted by the Office *twice*, in two separate cases, which resulted in issued U.S. Patent Nos. 5,977,316 and 5,935,821. The cited references are not enabling because disclosure of the name of the 11D10 hybridoma alone would not enable one skilled in the art to deduce the polynucleotide sequence encoding the heavy or light chain variable regions of 11D10, or fragments thereof, as presently claimed. Withdrawal of the §102(b) rejection evidences that the Office has deemed these references to be non-enabling for the claimed sequences. As such, these references do not provide a proper basis for a § 103 rejection of these claims.

Further, neither the hybridoma nor 11D10 antibody were provided to the public prior to the filing of the present application. Bhattacharya-Chatterjee et al. and Chakraborty et al. have been addressed in a previously-filed Declaration of Malaya (Bhattacharya-) Chatterjee. In her declaration, Dr. Chatterjee stated that the co-authors of these papers worked under her direct supervision, that the 11D10-producing hybridoma and 11D10 antibody remained under her strict supervision and control, that there had been no free exchange of 11D10 or the cell line producing 11D10, and that neither 11D10 nor the cell line producing 11D10 was released to the public prior to the filing of the present application. She expressly stated, "I did not make the antibody or cell line available to the public, and I did not believe I was under any obligation to make the antibody or cell line available." Declaration of Malaya Bhattacharya-Chatterjee, page 5. An identical statement was made in a declaration by Sunil Chatterjee. Declaration of Sunil Chatterjee, page 3. Likewise, in a Declaration by Kenneth Foon, Dr. Foon stated, "To the best of my knowledge and belief, the public did not obtain the 11D10 antibody-producing cell line or the 11D10 antibody, other than the participants in ...clinical studies..., at any time before the filing date of this patent application." Declaration of Kenneth Foon, page 2. All three of the above declarations were filed with the response to paper no. 15 and were also attached to the response to paper no. 24.

The Examiner states that the declarations of the inventors are "deficient" because they fail to "explicitly state how the hybridoma and the antibody were controlled by the declarer." Office Action, page 18. Applicants submit that it is not necessary for a declaration to set forth the precise means by which materials remain under the control of the declarer. In this instance, the declarations plainly state that the antibodies and hybridoma were not distributed to or provided to the public. That is the relevant question here, not the mechanism of such control. Both Malaya and Sunil Chatterjee expressly stated that they did not make the antibody or cell line available to the public. Declaration of Malaya Bhattacharya-Chatterjee, page 5; Declaration of Sunil Chatterjee, page 3. Malaya Chatterjee stated that she maintained strict and exclusive control over the distribution of the 11D10 antibody and the antibody producing cell line.

Declaration of Malaya Chatterjee, page 3. Similarly, Kenneth Foon expressly stated that the use and distribution of 11D10 for clinical trials was under his strict and exclusive control. Declaration of Kenneth Foon, page 2. The inventors all signed unequivocal statements indicating that they controlled the antibodies and cell line. The means of this control is irrelevant.

The Examiner also states that the declarations do not state that neither the hybridoma nor the antibody were publicly accessible or available upon request. Office Action, page 18. Applicants note that both Malaya Chatterjee and Sunil Chatterjee stated that they did not make the antibody or cell line available to the public and did not believe that they were under any obligation to do so (Declaration of Malaya Chatterjee, page 5; Declaration of Sunil Chatterjee, page 3), and Kenneth Foon stated that to the best of his knowledge and belief, the public did not obtain these materials (Declaration of Kenneth Foon, page 2). Thus, the declarations submitted are not deficient as the Examiner contends.[1]

35 U.S.C. §102(b) states, "A person shall be entitled to a patent unless the invention was . . . *in public use* . . . in this country, more than one year prior to the date of the application for patent in the United States." (emphasis added) Applicants do not agree or concede that the 11D10 antibody and hybridoma were accessible to the public. In addition, Applicants submit that whether the materials were accessible or available upon request is irrelevant in view of the fact that they were never actually provided to the public (*i.e.*, "in public use," as recited by the statute). In *Moleculon Research Corp. v. CBS, Inc.*, the Federal Circuit addressed the issue of whether an invention (a Rubic's cube puzzle) that had been shown to friends of the inventor was in public use prior to the filing of the patent application. The court affirmed the standard for public use as concerning whether or not an inventor has "at all times retained control over [an

[1] The Examiner also discusses typographical errors in the declarations of Malaya and Sunil Chatterjee, in particular a statement that "the public did have access to the cell line," and contends that these errors obscure the intent of the declarations. Office Action, pages 18-19. Applicants respectfully contend that these statements do not obscure the intent of the declarations, since the Examiner has acknowledged that these statements are "clearly the result of a typographical error." Office Action, pages 18-19. Thus, the intent and meaning of the declarations are clear.

invention's] use as well as over the distribution of information concerning it" 793 F.2d 1261, 1265. The *Moleculon* court also affirmed that "[t]he essence of 'public use' is the *free and unrestricted giving over* of an invention to a member of the public or the public in general." *Id.* (emphasis added). The court held that the invention was not in public use because it had remained under the inventor's control and had not been given over to others for their free and unrestricted use. *Id.* at 1266 (affirming the district court decision). 11D10 antibody was used in clinical trials. However, this was an experimental use, under inventor Kenneth Foon's "strict and exclusive control, and solely for purposes of administration to participants in the clinical trial(s)." Declaration of Kenneth Foon, page 2. In *Lough v. Brunswick Corp.*, the Federal Circuit affirmed that experimental use "to determine if the invention is suitable for its intended purpose" is not a public use. 86 F.3d 1113, 1120. The court held that in an experimental use analysis, the "factor of control is critically important." 86 F.3d 1113, 1120. In the present case, the inventors have explicitly declared that the 11D10 antibodies and hybridoma cell lines were retained under their exclusive control. Thus, the antibodies and hybridoma were not "in public use" prior to filing of the instant application.

In conclusion, neither Bhattacharya-Chatterjee et al. nor Chakraborty et al. teach polynucleotide sequences that encode polypeptide sequences of the light or heavy chain variable regions of antibody 11D10, and since neither the antibody nor the hybridoma which produces it were provided to the public prior to the filing date of the instant application, it would not have been possible for a person of skill in the art to obtain these sequences. The other cited references do not supply this missing element.

Kennedy et al. teaches that anti-idiotypic antibodies might be useful as vaccines and that chimeric versions of these antibodies may be produced. WO 94/11508 teaches anti-HMFG antibodies and polypeptides, and suggests methods for producing anti-idiotypic antibodies for HMFG. However, neither of these references teaches 11D10 antibody or the polynucleotide sequences encoding the light and heavy chain variable regions of 11D10 antibody.

Spooner et al. describe injection of polynucleotide expression vectors as anti-cancer vaccines, including injection of expression plasmids encoding the variable region genes of idiotypic antibodies to generate an anti-idiotypic immune response in the recipient. Stevenson et al. also teaches administration of an expression plasmid containing polynucleotide sequences encoding variable regions of idiotypic antibodies (the tumor antigens of B cell lymphomas) to generate an anti-idiotypic immune response in the recipient. Herlyn et al. teaches administration of an antiidiotypic antibody for a CRC (colorectal carcinoma)-associated antigen and compares the results to administration of a recombinant vector encoding the antigen itself. Neither Spooner, Stevenson, nor Herlyn teaches a recombinant vector that expresses an anti-idiotypic antibody, as asserted in the Office Action. Further, none of these references teach 11D10 antibody, polynucleotide sequences encoding the heavy or light chain variable regions of 11D10 antibody, or a polynucleotide encoding a polypeptide that is capable of eliciting an anti-HMFG immunological response in a mammal, as recited in the present claims.

In conclusion, the cited references do not render the instant invention unpatentable because the combination of references does not teach the specific polynucleotide sequences recited in the instant claims. Further, since neither the hybridoma that produces 11D10 nor the 11D10 antibody were provided to the public prior to the filing of this application, it would not have been possible for one of skill in the art to deduce these sequences.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Claims 6-12, 14-19, 38, 41, 44, 45, 57-66, and 70-80 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Chakraborty et al., 1995, *Cancer Research* 55:1525-1530, in view of Spooner et al., 1995, *Gene Therapy* 2:173-180, and Stevenson et al., 1995, *Immunological Reviews* 145:211-228, or Kennedy et al., 1985, *Biotechniques* 3:404-410, and

WO 94/11508-A2 (May 26, 1994), and in further view of Herlyn et al., 1995, *Hybridoma* 14:159-166. Applicants respectfully traverse this rejection.

To support a rejection under 35 U.S.C. §103(a), a reference must be available as prior art under §102 (MPEP § 2141.01). Applicants disagree with the Examiner's statement that Chakraborty et al. is available as prior art under § 102(a). As discussed in the response to paper no. 24, Chakraborty et al. is not a proper reference under § 102 because it represents work that was done under the direction of the inventors and was published less than one year prior to the filing of the present application. Applicants note that this reference was cited and withdrawn as a § 102 reference in related application U.S. serial no. 08/766,350, which has the same priority date as the instant application. The roles and contributions of the authors of the Chakraborty et al. reference have been addressed in the Declaration of Malaya Bhattacharya-Chatterjee, discussed above. This declaration shows that the Chakraborty et al. reference is not available as a § 102(a) or § 102(f) reference, and since it was published less than one year prior to the filing date, it is also not available as a § 102(b) reference. Therefore, Chakraborty et al. is not available as a supporting reference for a § 103(a) rejection since it is not a prior art reference under §102.

The Examiner states that the publication policy of *Cancer Research* rendered "the [11D10] antibody and the hybridoma . . . attainable, upon request, by any academic researcher, provided that the authors were willing and able to comply with the acknowledged and accepted policy of the journal." The Examiner further states that "[t]he fact that Applicants did not distribute the antibody or the hybridoma to any other person does not constitute evidence that the antibody and the hybridoma were not accessible or attainable upon request by another." Office Action, page 60. As discussed above, the *Cancer Research* paper has been previously addressed in the declaration by Malaya Chatterjee, filed with the response to paper no. 15, which explained that it represented the inventors' own work, which was performed under their supervision and control . In the interview of July 25, 2002, the Examiners stated that such a declaration would be sufficient to remove this reference, as well as the publication policy of *Cancer Research*, from consideration under §102(a).

In view of the previously-filed declaration of Malaya Chatterjee, the publication policy of *Cancer Research* is moot. However, for completeness, Applicants reiterate their previous position with respect to this policy. As discussed above, Applicants have expressly stated in previously-filed declarations that 11D10-producing hybridoma and 11D10 antibody remained under their control and had not been released to the public prior to the filing date of the present application. Even if the publication policy of *Cancer Research* were effective to render the antibody or hybridoma attainable upon request, which Applicants do not agree with or concede, the fact remains that the inventors never provided them to others. Applicants reiterate the point that *Cancer Research* merely has a *policy* that authors agree to make research materials available to others, but does not *require* authors to do so. In her declaration, Malaya Chatterjee expressly stated, "I did not make the antibody or cell line available to the public, and *I did not believe I was under any obligation to make the antibody or cell line available*" (p. 5, Declaration of Malaya Bhattacharya-Chatterjee, emphasis added). Despite the policy of *Cancer Research*, Dr. Chatterjee did not believe that she was obligation to provide these materials to others, and indeed did not do so. Further, even if, for the sake of argument, the publication policy of *Cancer Research* rendered the 11D10 antibody or hybridoma attainable by others, this did not occur before the invention by the Applicant. As discussed in the declaration by Malaya Bhattacharya-Chatterjee, the work published in the *Cancer Research* article was performed in her laboratory with the co-authors of the paper working under her direct supervision. Therefore, this publication did not appear before the invention by the Applicants, and since the publication policy of *Cancer Research* went into effect concurrent with publication, this policy likewise did not come into effect before the invention by the Applicants, removing it from the purview of §102(a). Logically, an antibody (or the hybridoma producing the antibody) could not become available until after it was produced.

A prima facie case for obviousness requires, *inter alia*, that prior art references, when combined, must teach or suggest all claim limitations (MPEP § 2143). The cited references do not teach, either singly or in combination, an isolated polynucleotide that encodes a polypeptide

comprising the three light chain or heavy chain CDRs of antibody 11D10, as recited in the present claims. Even if Chakraborty et al. were available as a prior art reference, Applicants reiterate their previous argument that this reference does not provide an enabling disclosure with respect to the instant claims, because disclosure of the 11D10 hybridoma alone would not enable one of skill in the art to deduce the claimed polynucleotide sequences. The other cited references do not supply this missing element.

Kennedy et al. teaches that anti-idiotypic antibodies might be useful as vaccines and that chimeric versions of these antibodies may be produced. WO 94/11508 teaches anti-HMFG antibodies and polypeptides, and suggests methods for producing anti-idiotypic antibodies for HMFG. However, neither of these references teaches 11D10 antibody or the polynucleotide sequences encoding the light and heavy chain variable regions of 11D10 antibody.

Spooner et al. describe injection of polynucleotide expression vectors as anti-cancer vaccines, including injection of expression plasmids encoding the variable region genes of idiotypic antibodies to generate an anti-idiotypic immune response in the recipient. Stevenson et al. also teaches administration of an expression plasmid containing polynucleotide sequences encoding variable regions of idiotypic antibodies (the tumor antigens of B cell lymphomas) to generate an anti-idiotypic immune response in the recipient. Herlyn et al. teaches administration of an antiidiotypic antibody for a CRC (colorectal carcinoma)-associated antigen and compares the results to administration of a recombinant vector encoding the antigen itself. Neither Spooner, Stevenson, nor Herlyn teaches a recombinant vector that expresses an anti-idiotypic antibody, as asserted in the Office Action. Further, none of these references teach 11D10 antibody, polynucleotide sequences encoding the heavy or light chain variable regions of 11D10 antibody, or a polynucleotide encoding a polypeptide that is capable of eliciting an anti-HMFG immunological response in a mammal, as recited in the present claims.

In conclusion, the cited references do not render the instant invention unpatentable because the combination of references does not teach the specific polynucleotide sequences recited in the instant claims. Further, as discussed above, since neither the hybridoma that

produces 11D10 nor the 11D10 antibody were provided to the public prior to the filing of this application, it would not have been possible for one of skill in the art to deduce these sequences.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Double Patenting

Claims 64, 65, and 71 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claim 1, 12, 23, and 24 of U.S. Patent 6,274,143-B1 in view of WO 94/11508-A2. Upon obtaining otherwise allowable subject matter, Applicants will file a terminal disclaimer in compliance with 37 C.F.R. § 1.321(c), thereby obviating this rejection.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the double patenting rejection.

CONCLUSION

Applicants have, by way of the amendments and remarks presented herein, removed the issues for the rejections and addressed all issues that were raised in the outstanding Office Action. Accordingly, reconsideration and allowance of the pending claims are respectfully requested. If it is determined that a telephone conversation would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 304142000322.

Respectfully submitted,

Dated: September 26, 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Please replace the paragraph beginning on page 5, line 20, with the following rewritten paragraph:

Figure 1 depicts the cDNA sequence (SEQ ID NO:1 and the amino acid sequence (SEQ ID NO:2) of the light chain variable region of 11D10 and adjoining residues. The CDRs and framework regions are indicated. There were clerical errors in Figure 1 as originally submitted. In the corrected figures, [T]the correct translation [should] shows A, or alanine, for amino acid -18, and E, or glutamic acid for amino acid 81 (SEQ ID NO:2).

Please replace the paragraph beginning on page 5, line 26, with the following rewritten paragraph:

Figure 3 depicts the amino acid sequences of the light chain variable region (Amino acids 1-107 of SEQ ID NO:2; Fig. 3A) and the heavy chain variable region (Amino acids 1-118 of SEQ ID NO:4; Fig. 3B) of 11D10. Each variable region consists of 4 framework regions and 3 CDRs. There was a clerical error in Figure 3A as originally submitted. For Figure 3A, the correct translation [should] shows E, or glutamic acid, for amino acid 81.

Please replace the paragraph beginning on page 69, line 15, with the following rewritten paragraph:

In Figure 1 as originally submitted it is clear that the third amino acid of the leader sequence (amino acid -18) and the twenty-fifth amino acid of framework 3 (amino acid 81) are in error. As is readily apparent to one skilled in the art, the amino acid encoded by the nucleotide triplet "GCC" is A, or alanine (for amino acid 81). Likewise, in Figure 3A as originally submitted, amino acid 81 (within framework 3) is E, or glutamic acid. SEQ ID NO:58 depicts the incorrect amino acid translation as shown by the typographical errors on the typed sheet

reading "Figure 1" that [has been] was originally submitted with this disclosure. SEQ ID NO:2 depicts the correct amino acid translation shown in the corrected figures.

In the Claims:

Please amend claims 6, 9, 10, 14, 15, 19, 44, 57-59, 65, 69, 70, 72, 73, and 79 as follows:

6. (Once Amended) An isolated polynucleotide comprising a sequence encoding a polypeptide that is capable of eliciting an anti-HMFG immunological response in a mammal, wherein the polypeptide comprises an immunoglobulin variable region containing the three light chain complementarity determining regions (CDRs) of antibody 11D10 or an immunoglobulin variable region containing the three heavy chain CDRs of antibody 11D10, wherein antibody 11D10 is produced by the hybridoma deposited under ATCC Accession No. HB-12020 [or progeny thereof].

9. (Once Amended) A polynucleotide according to claim 6, wherein the immunoglobulin light chain variable region is contained in SEQ ID NO:2.

10. (Once Amended) A polynucleotide according to claim 6, wherein the immunoglobulin heavy chain variable region is contained in SEQ ID NO:4.

14. (Thrice Amended) An isolated polynucleotide comprising a region of at least 100 contiguous nucleotides of the sequence contained in SEQ ID NO:1.

15. (Thrice Amended) An isolated polynucleotide comprising a region of at least 75 contiguous nucleotides of the sequence contained in SEQ ID NO:3.

19. (Once Amended) A host cell comprising the polynucleotide of claim 6[, wherein the polynucleotide is a recombinant polynucleotide].

44. (Once Amended) The immunogenic composition of claim 41, wherein the polynucleotide is comprised in a live recombinant virus or viral expression vector.

57. (Twice Amended) A kit for detection or quantitation of [a polynucleotide comprising] a polynucleotide which comprises a sequence encoding a variable region of antibody 11D10 or a portion thereof, said kit comprising the polynucleotide of claim 14 in [suitable] packaging.

58. (Twice Amended) A kit for detection or quantitation of [a polynucleotide comprising] a polynucleotide which comprises a sequence encoding a variable region of antibody 11D10 or a portion thereof, said kit comprising the polynucleotide of claim 15 in [suitable] packaging.

59. (Once Amended) The polynucleotide of claim 6, wherein [antibody 11D10] the polypeptide has the light and heavy chain variable region sequences contained in SEQ ID NO:2 and SEQ ID NO:4, respectively.

65. (Once Amended) A polynucleotide according to claim 64, wherein the variable regions are joined by a [linked] linker polypeptide of about 5 to 20 amino acids.

69. (Once Amended) A method of preparing a heavy chain variable region of antibody 11D10 [comprising variable region of antibody 11D10] comprising expressing the polynucleotide of claim 73 in a host cell.

70. (Once Amended) A kit for eliciting an anti-HMFG immunological response in a mammal comprising the polynucleotide of claim 6 in [suitable] packaging.

72. (Once Amended) An isolated polynucleotide encoding an immunoglobulin variable region containing the three light chain CDRs in SEQ ID NO:2.

73. (Once Amended) An isolated polynucleotide encoding an immunoglobulin variable region containing the three heavy chain CDRs in SEQ ID NO:4.

79. (Once Amended) A composition according to any of claims 38, 41, 44, 45, [60, 61,] or 66[, or 76], wherein the polynucleotide is a recombinant polynucleotide.